

# Neurocase

## The Neural Basis of Cognition

ISSN: 1355-4794 (Print) 1465-3656 (Online) Journal homepage: <https://www.tandfonline.com/loi/nncs20>

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To cite this article: Adelle G.B. Cerreta, Timothy J. Vickery & Marian E. Berryhill (2018) Visual statistical learning deficits in memory-impaired individuals, *Neurocase*, 24:5-6, 259-265, DOI: [10.1080/13554794.2019.1579843](https://doi.org/10.1080/13554794.2019.1579843)

To link to this article: <https://doi.org/10.1080/13554794.2019.1579843>



Published online: 22 Feb 2019.



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## Visual statistical learning deficits in memory-impaired individuals

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### ABSTRACT

Visual statistical learning (VSL) refers to the learning of environmental regularities. Classically considered an implicit process, one patient with isolated hippocampal damage is severely impaired at VSL tasks, suggesting involvement of explicit memory. Here, we asked whether memory impairment (MI) alone, absent of clear hippocampal pathology, predicted deficits across different VSL tasks. A classic VSL task revealed no learning in MI participants (Exp. 1), while imposing attentional demands (Exp. 2: flicker detection, Exp. 3: gender/location categorization) during familiarization revealed modest residual VSL. MI with nonspecific neural correlates predicted impaired VSL overall, but attentional processes may be harnessed for rehabilitation.

### ARTICLE HISTORY

Received 13 September 2018  
Accepted 31 January 2019

### KEYWORDS

Visual statistical learning;  
traumatic brain injury;  
memory impairment;  
amnesia; episodic memory

### Introduction

Regular co-occurrence of events, words, or images in the environment enables prediction (Fiser & Aslin, 2002; Saffran, Aslin, & Newport, 1996). Statistical learning (SL), the detection of environmental regularities, is evident in non-human species (Doupe & Kuhl, 1999; Meyer & Olson, 2011; Toro & Trobalon, 2005) and in human infants engaged in language learning and reading (Fiser & Aslin, 2002; Sigurdardottir et al., 2017). Interpreting environmental regularities is therefore an important part of processing the environment. Classically, SL is considered an implicit learning process not requiring instruction nor conscious awareness (Aslin & Newport, 2012; reviewed in: Aslin, 2017). Participants receive no explicit instructions regarding the embedded probabilities, yet they correctly recognize familiarized pairings after repeated exposures. Indeed, neuropsychological support for the predominantly implicit view was found when amnesic participants with medial temporal lobe or diencephalic damage performed similarly to controls in a probabilistic learning task (Knowlton, Squire, & Gluck, 1994), and patients with medial temporal lobe damage showed preserved implicit category learning (Bayley, Frascino, & Squire, 2005). Two studies even reported superior performance on implicit category learning tasks in MI participants (Dienes, Baddeley, & Jansari, 2012; O'Connell et al., 2016).

However, recent fMRI findings raise questions regarding the implicit nature of SL by observing activity in medial temporal lobe regions including the hippocampus *during* SL (Giorgio et al., 2017; Turk-Browne, Scholl, Chun, & Johnson, 2009). Secondly, a rare patient with bilateral hippocampal damage demonstrated profound visual statistical learning (VSL) impairment (Schapiro, Gregory, Landau, McCloskey, & Turk-Browne, 2014; Schapiro & Turk-Browne, 2015). Revisiting the earlier Knowlton et al. (1994) study of probabilistic learning in amnesics showed that they did perform worse than controls after delayed testing. A meta-analysis of 12 implicit category learning studies also identified a significant deficit in MI participants (Zaki, 2004). These data

promoted the interpretation that SL, or at least some SL tasks, require dual forms of memory: implicit and explicit. Furthermore, there are important anatomical hippocampal-striatal connections (Durrant, Cairney, & Lewis, 2012; Johnson, van der Meer, & Redish, 2007; Pennartz, Ito, Verschure, Battaglia, & Robbins, 2011) that may underlie interactions between implicit and explicit forms of memory (Ashby, Alfonso-Reese, Turken, & Waldron, 1998; Reber, Knowlton, & Squire, 1996; Zaki & Nosofsky, 2001).

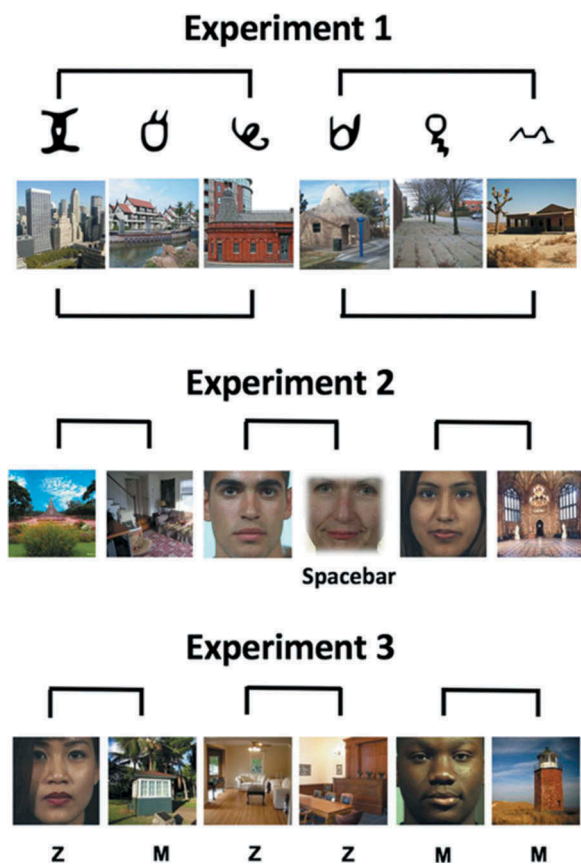
The striatum could also have important contributions to SL. It has known involvement in procedural memory and habit-learning (Yin & Knowlton, 2006; for review see: Seger & Spiering, 2011), and responds to structured coincidence or sequences (Grafton, Hazeltine, & Ivry, 1995; Karuza et al., 2013; Meck, Penney, & Pouthas, 2008; Turk-Browne et al., 2009), implying involvement with VSL. Further, an interplay between striatum and hippocampus is implicated in memory formation, demonstrating that these regions can acquire corresponding information concurrently (Doeller, King, & Burgess, 2008; McDonald & White, 1993, 1994; Poldrack et al., 2001). Indeed, modeling by Moustafa, Keri, Herzallah, Myers, and Gluck (2010) predicts that neurotransmitter loss in either the hippocampus (acetylcholine) or the striatum (dopamine) impairs learning. However, recent evidence suggests a connection between the striatum and explicit awareness, – its activity is linked to the emerging explicit awareness of a sequence (Clos, Sommer, Schneider, & Rose, 2018; Rose, Haider, & Buchel, 2010). Thus, evidence conclusively tying striatum with implicit and hippocampus with explicit memory formation is muddled.

Recent behavioral findings raise additional questions regarding attentional contributions to VSL. The familiarization, or “cover”, task implemented during VSL acquisition influences the kinds of associations learned and subsequent behavior (Bays, Turk-Browne, & Seitz, 2015). Recently, we reported that imposing a categorization demand during the familiarization task (gender/location) interfered with VSL. This interference arose when neurotypical participants had to press a *different*

key or make a *different* judgment during the A-B pair (Vickery, Park, Gupta, & Berryhill, 2018). These observations confirm that attention affects VSL and might be leveraged to rescue performance in clinical populations. In the following studies, we examined whether episodic memory impairment (MI) alone, without clear hippocampal (or striatal) damage impairs VSL performance. In other words, if VSL is purely implicit for these tasks, the MI group should perform normally, and be impaired if explicit memory is contributing. Furthermore, if the MI individuals are impaired we test whether increasing the attentional demands of the VSL familiarization task can improve their performance.

Experiments 1–3: overview

The protocol for Experiment 1 followed that of Turk-Browne et al. (2009), and Experiments 2 and 3 followed Vickery et al. (2018); see Figure 1. The key analysis compared neurotypical with MI performance. The same control and MI patient participants provided data for Experiments 1–3. Groups were age-matched and education-matched, with control participants recruited from the University of Nevada and surrounding community. MI participants were recruited from a local head injury support group seeking those whose primary deficits were memory-related. Task order was counterbalanced across participants. Protocols were approved by the University of Nevada IRB. Participants signed informed consent documents and were reimbursed \$10/hour.



**Figure 1.** Design of the familiarization phase for each experiment. Stimuli were presented sequentially with repeating triplets (Experiment 1: scenes, shapes) or pairs (Experiments 2–3: faces, scenes). The familiarization task was passive viewing (Experiment 1), flicker detection (Experiment 2), or categorization of images (male/female, indoor/outdoor). Correct key presses are indicated: “Z”, “M”, and “Spacebar”. Brackets indicate the familiarized sequences (triplets or pairs).

Participants

**Neurotypical participants.** 34 neurotypical adults contributed data. We tested a younger group (N = 17, mean age: 20.8 years, 15.1 years of education, matching S1) and an older control group (N = 17, mean age: 33.9 years, 14.2 years of education, matching BN1 and XX). We collapsed the groups as they showed no performance differences (all *ps* > .4).

**MI participants.** MI participants completed two sessions per experiment on different days. Novel SL combinations were used each session. None remembered having previously completed any session. MI group injuries and symptoms were heterogeneous, but all exhibited significant memory deficits; see Table 1. General cognitive assessments revealed that 2 of the 3 MI participants also showed broader cognitive impairment.

**BN1.** BN1 is a 37-year old woman with 12 years of education. Seven years ago, she had an anoxic event following a withdrawal-induced seizure. Cardiac arrest was followed by a 10-minute anoxic period and 2-weeks on life support. She is currently healthy and stable. She has an implanted defibrillator making MRI impossible; acute CT scans were unremarkable. She is ambidextrous and prefers to write with her left hand. Her vision is uncorrected and she was compliant and motivated with a positive, pleasant affect. She is physically active, regularly skiing and golfing. She engages in daily cognitive training (Lumosity, Constant Therapy). On the Mini-Mental Status Exam (MMSE) she was unable to name the date and forgot all three words at delayed recall. A 2015 neuropsychological report noted deficits in sustained attention, processing speed, executive function, and full-scale IQ. Language and visual perception are relatively spared (see Table 1). She was able to describe one episodic memory from her lifetime during Levine’s Autobiographical Memory Test (Levine, 2004). Her scores on the WAIS-IV fell at or below the 30th percentile. To further probe executive function, we conducted the Hayling and Brixton tests (Burgess & Shallice, 1997) and observed low-average and moderate-average performance, respectively. Her performance on the Warrington Recognition Memory Test (Warrington, 1984) was at chance for delay. BN1’s primary deficit is episodic memory with WMS scores falling at or below the 1st percentile; see Table 1.

**Table 1.** Neuropsychological test scores for patients BN1, XX, and S1. Scores are presented as percentile index scores. Italicized values fall below the normal range. MMSE: mini-mental status examination, WMS-IV: Wechsler Memory Scale, 4th edition (Wechsler, 2009).

Test	Subscale	BN1	XX	S1
MMSE		25	25	27
Pyramids & Palm Trees (>47)		46	49	50
Benton’s Face Recognition (>44)		51	44	40
WMS-IV				
	<i>Auditory Memory</i>	<.1	1	.1
	<i>Visual Memory</i>	<.1	<.1	2
	<i>Visual Working Memory</i>	1	2	21
	<i>Immediate Memory</i>	1	.1	1
	<i>Delayed Memory</i>	<.1	.2	.1

**XX.** XX is a 32-year old male with 12 years of education. One year before testing he fell off a ladder while installing a satellite dish. After many hours, he went to the emergency room and was diagnosed with traumatic brain injury (TBI) and thrombosis. His MRI and radiology reports identify no abnormalities. He is bothered by his memory deficits. He has periodic seizures believed to be caused by his TBI and exacerbated by cognitive effort. His wife and children are his main support, and he enjoys watching sports. XX's performance on Warrington's Recognition Memory test was 44/50 (88%) for words, and 33/50 (66%) for faces. His WASI-II percentile rankings were universally low (verbal comprehension: 14%, reasoning: 1%, full scale-4: 4%, full-scale-2: 4%). Importantly, his episodic memory is impaired, with WMS scores falling at or below the 2nd percentile.

**S1.** S1 is a 19-year old female with 12 years of education. At age 11, she suffered a TBI after being hit by a car while crossing in a crosswalk. She spent one month in an intensive care unit in a medically-induced coma. Her family pursues all rehabilitation opportunities, including at-home hyperbaric oxygen treatment. She graduated from a special education program. She is optimistic and social. She reports her primary cognitive deficits are memory-related and she relies heavily on her smartphone. Her performance on the WASI-II showed normal percentile rankings (verbal comprehension: 77%, reasoning: 79%, full scale-4: 81%, full-scale-2: 84%). Performance for words on Warrington's Recognition Memory test was 49/50 (98%), and for faces was 34/50 (68%). S1's primary complaint is episodic memory with WMS scores falling at or below the 2nd percentile, except for better preserved visual working memory (21st percentile).

## Experiment 1: VSL triplets

### Methods

#### Stimuli

The protocol followed Turk-Browne et al. (2009). There were two stimulus categories: shapes and scenes. Shapes (200 x 200 pixels) consisted of 12 Ndjuka symbols (Rogers, Friedman, & Vickery, 2016; Turk-Browne et al., 2009).

Scenes (250 x 250 pixels) consisted of 12 indoor and outdoor images. Stimuli were presented using Matlab and the Psychophysics Toolbox (Brainard, 1997) on a 15.4" MacBook Pro monitor (resolution: 1440 x 900) against a white background at a distance of 57 cm. Triplets were randomly assigned per participant and session, without replacement to one of four sets (Fiser & Aslin, 2002; Saffran et al., 1996). Foils were constructed the same way but only appeared at test.

### Procedures

#### Familiarization phase

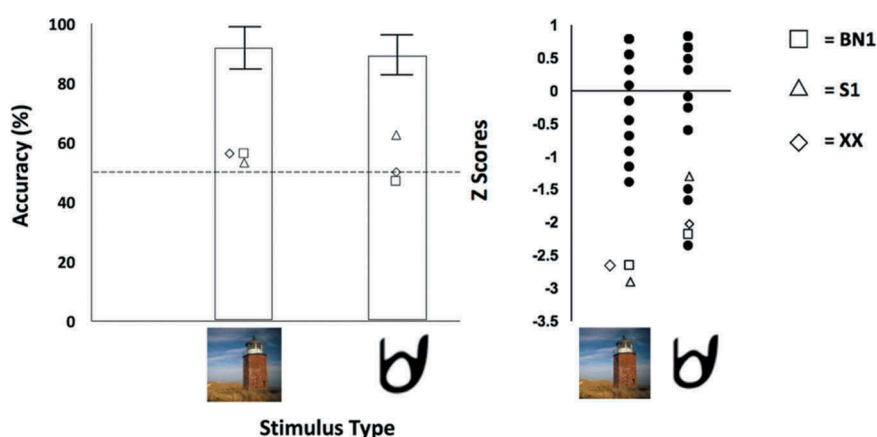
Participants were instructed to attend to sequentially-presented stimuli (0.5 s/image, 0.5 s ISI), but not informed of the repeating triplets. Participants viewed 4 triplets 24 times for a total of 96 presentations per stimulus category.

#### Recognition phase

After familiarization, participants answered 32 two-alternative forced-choice trials. First, "Sequence 1" appeared slightly left of center, followed by a sequence presented left of center. Next the words "Sequence 2" appeared slightly right of center, followed by a second triplet slightly rightward. Participants were instructed to select the "more familiar" triplet using the left (Sequence 1) and right (Sequence 2) arrow keys (50% chance). The task lasted ~11 minutes per category.

### Results

Controls exhibited above-chance VSL for both stimulus categories (one-sample t-test versus chance: scene:  $t_{33} = 18.34$ ,  $p < .001$ ,  $d = 3.13$ ; shape:  $t_{33} = 11.89$ ,  $p < .001$ ,  $d = 2.05$ ; see Figure 2). Each MI participant showed significant impairment in one (S1) or both (BN1, XX) categories; see Table 2. In S1's case, in the other category she showed a borderline deficit ( $z = -1.3$ ).



**Figure 2.** Experiment 1 Triplet Task Results. Left: Behavioral results from the recognition phase after passive familiarization. Bar plots indicate mean control performance and the error bars show 95% confidence intervals. Data points are jittered for clarity. Controls performed significantly better than MI participants. The dashed line marks chance performance (50%). Right: Data represent each participant's z-scores for each category.

## Experiment 2: VSL flicker detection familiarization task

Experiment 1 revealed general VSL deficits in the MI participants in a standard task that generalized across two types of stimuli. One interpretation is that VSL performance depends to some extent on explicit memory because deficits in explicit memory impaired VSL ability. If true, increasing the attentional demands of the task might enable VSL performance by supporting residual explicit memory or by supporting implicit memory. In Experiment 2, this involved imposing an attentional demand – to respond via button press when a stimulus flickered.

### Methods

#### Stimuli

The protocol followed Vickery et al. (2018). The stimuli were color images (200 x 200 pixels) of faces expressing neutral emotions selected from the Face Recognition Technology (FERET) database (Phillips, Wechsler, Huang, & Rauss, 1998), and color images of indoor/outdoor scenes (200 X 200 pixels) selected from the internet.

#### Procedures

##### Familiarization

Images were grouped into 16 AB pairs, defined per session: within-category (face-face, scene-scene) or cross-category (face-scene, scene-face). No pair immediately repeated (1 s/image, 1 s ISI). Pairs consisted of distinct combinations of each category (e.g., 4 different male faces were paired with and followed by a different female/male/interior/exterior image). 16 singleton images (4 per image type) were presented

without a B complement. Participants were instructed to attend and to press the spacebar when an image “flickered”. On 25% of trials the image briefly extinguished (53.3 ms) 453.3 ms post-onset. There were 960 trials per session, lasting ~30 minutes.

#### Recognition

In 64 forced-choice trials participants viewed two AB pairs presented sequentially (labelled “Sequence 1” or “Sequence 2”, 0.5 s, 0.5 s ITI). They reported via key press the familiar pair (50% chance). Foils were created by maintaining AB positions but swapping across pairs. Each target pair was tested 4 times.

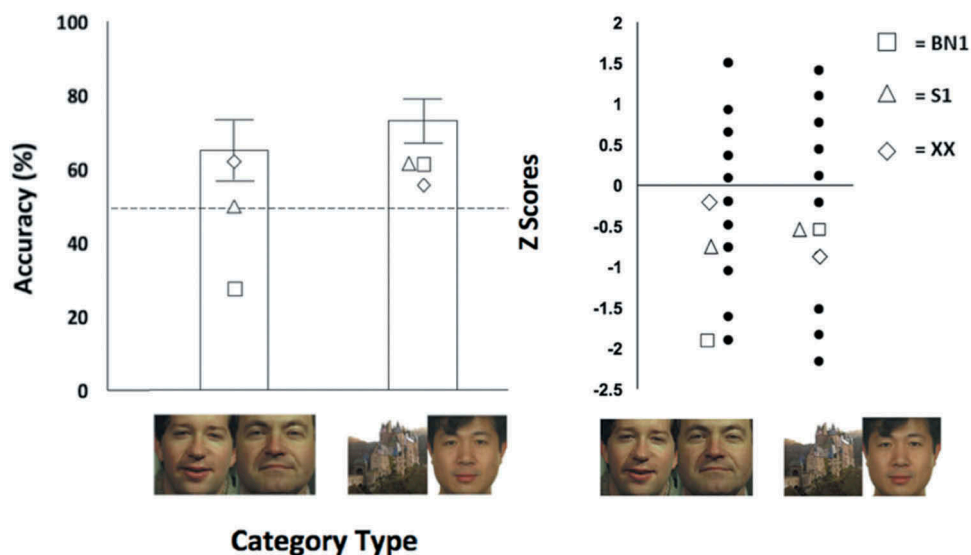
### Results

#### Familiarization phase

Reaction times were analyzed to ensure consistent performance across all stimuli. Control participants’ median reaction time to flickers was 0.45 s (standard deviation: .06 s, mean hit rate of .98, false alarm rate of .01). The MI participants performed similarly: (median reaction time: 0.56 s, standard deviation: 0.01 s). Hit rate and false alarm rates were similar, and are indicative of sustained attention on the task (BN1: .96, .01, XX: .93, .01, S1: .99, .01).

#### Recognition phase

Control group recognition was universally above chance (one-sample t-tests:  $t_{33} > 4.51$ ,  $p_s < .001$ ,  $d_s > 0.77$ ); see Figure 3. After normalizing MI performance using the control distribution, the MI patients’ z-scores were largely  $< -1$ , indicating that they were not grossly impaired; see Table 2. In MI individuals, VSL might be rescued by changing the familiarization task demands.



**Figure 3.** Experiment 2 recognition accuracy (Left) and z-score (Right) data. Pairs consisted of the same category (face-face; left) or different categories (scene-face; right). The dashed line reflects chance performance: 50%. The error bars reflect the 95% confidence intervals.



### Experiment 3: categorization familiarization task

Experiment 2 provided evidence that VSL is not purely implicit. Importantly, it suggested that heightening attentional demands during familiarization might further support VSL in MI individuals. We investigated whether further increasing the attentional demands during the familiarization task would further benefit VSL in the MI group. Experiment 3 required the categorization (male/female, indoor/outdoor) of every stimulus presented during familiarization.

### Methods

The stimuli from Experiment 2 were used, but participants categorized image gender (male/female) or scene (indoor/outdoor) via key press (male/outdoor: "m", female/indoor: "z"). A notecard with response mappings was provided. Trials were divided to reflect the categorization judgment and responses during familiarization. The trials were termed: *Same Task, Same Response* ( $S_T S_R$ ; a within-category pair with matching responses, e.g., Female Face-Female Face), *Same Task, Different Response* ( $S_T D_R$ ; a within-category pair with different responses, e.g., Female -Male Faces), *Different Task, Same Response* ( $D_T S_R$ ; a cross-category pair with matching responses, e.g., Female Face-Indoor Scene), and *Different Task, Different Response* ( $D_T D_R$ ; a cross-category pair with different responses, e.g., Female Face-Outdoor Scene). There were 4 pairs of each of the trial type, uniquely constructed per session.

### Results

#### Familiarization phase

The control group responded quickly (median reaction time of .56 s, standard deviation: .06 s) and accurately (.97). The MI participants were slower (BN1: 0.78 s, S1: 0.59 s, XX: 0.70 s), but accurate (BN1: .96, S1: .84, XX: .90).

#### Recognition

Replicating previous results (Vickery et al., 2018; see Figure 4), control participants exhibited a significant difference in

performance (2 response (same, different) X 2 categorization task (same, different) repeated measures ANOVA in terms of response type ( $F(1,33) = 15.77, p < .001, \eta_p^2 = 0.32$ ) and category type ( $F(1,33) = 16.36, p < .001, \eta_p^2 = 0.33$ ), but no interaction ( $F(1,33) = 1.71, p = .201, \eta_p^2 = 0.05$ ). VSL performance was above chance on three trial types: ( $S_T S_R$ : one-sample t-test:  $t_{33} = 7.35, p < .001, d = 1.26$ ;  $S_T D_R$ :  $t_{33} = 3.45, p = .002, d = 0.59$ ;  $D_T S_R$ :  $t_{33} = 2.63, p = .013, d = 0.45$ ), but no different from chance on  $D_T D_R$  trials ( $t_{33} = .97, p = .34, d = 0.17$ ).

MI participants showed heterogeneous response patterns. All had some positive z-scores, and some in the borderline ( $> -1$ ) or impaired range ( $> -1.96$ ). BN1 and XX were significantly impaired on  $S_T S_R$  trials, opposite the pattern observed in controls. S1 showed normal performance across conditions with borderline impairment on the  $D_T S_R$  condition. All MI participants demonstrated above chance VSL on the  $D_T D_R$  condition, whereas controls did not.

**Table 2.** Individual MI patient performance across studies. MI participants' z-scores compared to the control group for each experiment (z-scores were comparable to Crawford-Howell t-test values (Crawford & Howell, 1998)). Italicized values surpass 95% confidence intervals ( $>1.96$ ) and mark significant impairment. Abbreviations as in Figure 4.

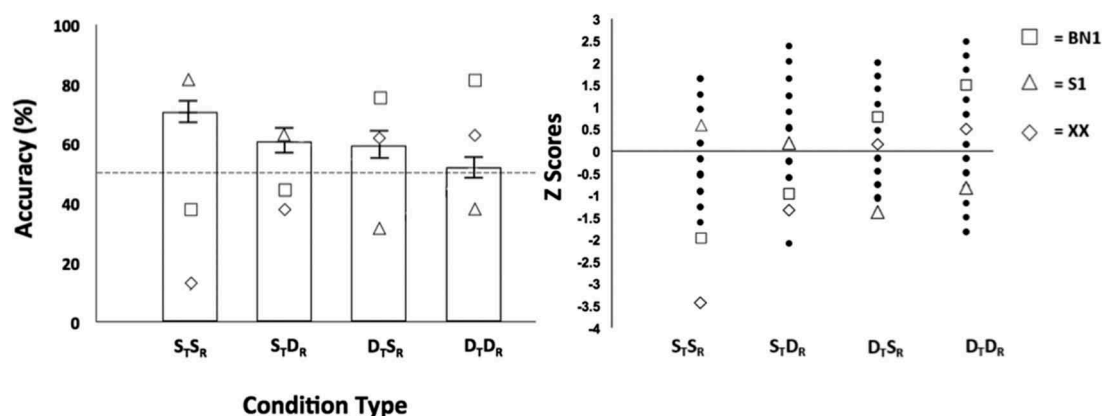
	Exp. 1	Exp. 2	Exp. 3			
	Stimulus Type (Scene/Shape)	Category Type (Same/Different)	$S_T S_R$	$S_T D_R$	$D_T S_R$	$D_T D_R$
BN1	<b>-2.67; -2.21</b>	<b>-1.90; -0.55</b>	<b>-1.99</b>	-0.96	0.76	1.47
XX	<b>-2.67; -2.04</b>	-0.21; -0.87	<b>-3.44</b>	-1.34	0.16	0.50
S1	<b>-2.90; -1.30</b>	-0.77; -0.55	0.56	0.15	-1.37	-0.83

#### Control analysis

We tested controls in several VSL studies raising the concern that they employed explicit learning strategies. Concern was mitigated by the null findings in an analysis of performance by task order (1st M(SD): 0.76(.19), 2nd: 0.73(.21), 3rd: 0.70(.16);  $F(2,66) = 0.568, p = .569, \eta_p^2 = 0.14$ ).

#### General discussion

These experiments provided support for the possibility that attentional manipulations might be a tool for improving VSL in



**Figure 4.** Experiment 3 behavioral results: accuracy (Left), z-scores (Right). Abbreviations:  $S_T S_R$  = same task, same response;  $S_T D_R$  = same task, different response;  $D_T S_R$  = different task, same response;  $D_T D_R$ : different task, different response. Data points are jittered for visibility. The dashed line reflects chance recognition performance (50%). The error bars reflect the 95% confidence intervals for the control participants.

the MI population. It also is consistent with the view that VSL involves both implicit and explicit forms of memory. MI participants showed no VSL in the triplet learning task (Experiment 1). Importantly, requiring sustained attention to detect a stimulus flicker during familiarization appeared to modestly improve VSL (Experiment 2). But when the familiarization task required image categorization the data provided a heterogeneous pattern of VSL without consistent evidence of residual VSL, nor the categorization interference observed in controls (Experiment 3). VSL in the MI population is impaired, but there may be a possibility of mitigating VSL by increasing the attentional demands during familiarization. The current data identify VSL impairment in MI individuals even when they lack clear hippocampal damage. This extends recent findings showing VSL impairment after hippocampal damage (Covington, Brown-Schmidt, & Duff, 2018; Schapiro et al., 2014).

The engagement of implicit and explicit processes in SL are beginning to be studied (Batterink, Reber, Neville, & Paller, 2015; Dale, Duran, & Morehead, 2012). Attentional manipulations may improve performance by making stimuli more salient and more likely to be familiarized via interactions between implicit and explicit processes (Andringa & Rebuschat, 2015). Understanding these interactions may be valuable in adjudicating between unitary and multiple memory theories (Ashby et al., 1998; Reber et al., 1996; Zaki & Nosofsky, 2001). Identifying the neural correlates of implicit-explicit memory interactions will likely require a deeper accounting of hippocampal and striatal interactions. The work presented here cannot dictate definitive statements regarding neural correlates of the resulting behavior, but we propose that performance altered as a function of task due to the selective deployment of attention. Our data are consistent with possibility that in these MI participants remaining hippocampal-striatal connections and attentional manipulations might be leveraged to improve their VSL ability.

We close by posing a different type of question: Is it useful to improve VSL? We argue, along with others, that VSL facilitates prediction and remains relevant over the life-span (reviewed in: Siegelman & Frost, 2015). Thus, our view is that addressing VSL loss after MI is clinically relevant and feasible given the modest attentional manipulations that seemed to support remaining VSL abilities. Subject-specific injury factors must be considered for each participant tested, as implicit and explicit strategies of learning are dependent on the person (Smith, Urgolites, Hopkins, & Squire, 2014). Finally, we acknowledge that we were limited by a small number of MI participants, two of whom also had other cognitive impairments. We also would not retest controls going forward. In closing, we propose that it is incumbent upon rehabilitation specialists to address VSL deficits in the MI population.

## Acknowledgments

This research was funded by NSF OIA 1632849 to TJV and MEB, NSF BCS 1558535 to TJV, and NSF OIA 1632738 to MEB.

## Disclosure statement

No potential conflict of interest was reported by the authors.

## Funding

This work was supported by the National Science Foundation [BCS 1558535, OIA 1632738, OIA 1632849].

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